THE CORRELATION BETWEEN THE TRANSITION METALS AND PULMONARY FUNCTION TEST WITH CLUB CELLS IN WOMEN COOKING USING BIOMASS FUEL

SYNOPSIS

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Introduction

In India, 41% of people use only wood for cooking and heating purposes[1]. The fuel is classified as solid fuel – coal and biomass fuels and non-solid fuel – Kerosene, Liquefied petroleum gas, Gas, and Electricity. While combustion of biomass fuel, various pollutants were released. The pollutants were classified as gaseous such as formaldehyde, carbon monoxide, polyaromatic hydrocarbon, nitrogen oxides, sulphur, ammonia, and particulate matter (PM0.1, PM2.5, and PM10) which is based on aerodynamic diameter[2].

Metal can be defined as "an element which under biologically significant conditions may react by losing one or more electrons to form cations". Various metals are released from occupation and non-occupational exposure/household environment during several processes like cooking, burning of coal, welding, mining etc. Humans can be exposed to biomass pollutants via inhalation, dermal, or ingestion.

The transition metals have different characteristics such as various oxidation states, nature of their ligands, solubility, structure of the molecule, particle size, and surface area per mass of metals[3], at various concentrations in serum, metals affect the respiratory system, cardiovascular system, nervous system, etc., in the human body which can cause genotoxicity, ARDS, metal fume fever, dysfunction of alveolar cells, lesion in membrane of the alveoli.

The respiratory system consists of the conducting zone (trachea, bronchi, and bronchioles) and the respiratory zone (respiratory bronchioles, alveolar ducts and pulmonary alveoli). Ciliated cells, microvillar cells, small granule cells, bronchiolar cells/club cells/clara cells were present in respiratory

bronchioles. In 1937, Leipzig anatomist Max Clara described a new secretory cell type in the human bronchial epithelium. Club cells are associated with important functional activities such as cellular proliferation, and the biosynthesis, storage, and release of various secretory products.

Nearly 11-22% of dome-shaped, non-ciliated cells are located in the respiratory bronchioles of the respiratory system. The club cells synthesize CC-16 protein, its molecular mass is 16,000 Daltons, under the Subfamily of secretoglobin, it is a homodimer consisting of 70 amino acids in antiparallel arrangement and connected by two disulfide bonds. The concentration of CC16 protein in pulmonary fluid (bronchoalveolar lavage fluid -BALF 0.5 to 1.5 mg/L and epithelium lining fluid -ELF 100 mg/L) and extrapulmonary fluid (serum 5 to 50 μg/L). Club cells have the highest levels of cytochrome P_{450} oxidases, which are involved in anti-inflammatory, anti-neoplastic activity, anti-fibrotic activity, and immunomodulatory, cellular proliferation, biosynthesis, storage, the release of various secretory products, detoxifying xenobiotics in human lung, immunosuppressive[4].

CC-16 protein is a new tool and sensitive biomarker to evaluate the permeability of the lung epithelial barrier when exposed to indoor air pollutants.

Aim and Objective

To determine the effect of transition metals on pulmonary function test and CC16 protein secretion in healthy adult rural women using biomass fuel for more than five years compared to those who do not.

Secondary Objective

1. To compare the transition metals levels in biomass fuel users and clean fuel users
2. To compare the pulmonary function and serum CC16 levels in biomass fuel users and clean fuel users.

Hypothesis

Among rural women using biomass fuel for more than five years increase in transition metals reduces club cell protein secretion and pulmonary function compared to those not using biomass fuel.

Review of Literature

With prolonged usage of biomass fuel for cooking, women are easily exposed to biomass smoke. The duration of exposure to biomass smoke is termed as biomass exposure index (BEI), which is calculated as the average hours spent during daily cooking multiplied by the number of years and expressed as hour-years.

The biomass fuel releases various ions at different concentrations during the combustion of wood[5] which are present in indoor air such as Cl^-, NO_3^-, SO_4^{2-}, NH_4^+, Na^+, K^+, Mg^{2+}, and Ca^{2+}. The transition metals of mercury, cadmium, chromium, nickel, and zinc are present in biomass smoke as pollutants in various concentrations.

Many previous studies mention the effect of biomass smoke on forced vital capacity (FVC), forced expiratory volume in 1st second (FEV_1), FEV_1/FVC ratio, forced mid-expiratory flow ($FEF_{25-75\%}$), peak expiratory flow rate (PEFR). The pulmonary function test declines in women who are exposed to biomass smoke due to high levels of indoor air pollution concentration with poor ventilation[6] and high concentrations of metals[7].

The club cell protein secretion alters either increasing or decreasing in serum concentration due to prolonged exposure to biomass smoke, it reflects hyperpermeability of the alveolar-capillary barrier or cytotoxicity of club cells in bronchioles[8]. In animal studies, the CC16-/- mice show airway morphology changes, increased inflammatory cells, and increased activation of NF-κB and $sPLA_2$ indicating CC16 is involved in a protective role[9]. The level of S-CC16 protein concentration altered among chronic obstructive pulmonary diseases

(COPD), acute respiratory distress syndrome (ARDS), and idiopathic pulmonary fibrosis (IPF), indicates potential biomarkers for prognostic and differential diagnosis[10].

Methodology

This study is a population-based cross-sectional study and this was conducted in Kundrathur and Kadampadi village, Kancheepuram district from 2018 to 2019 after being approved by the Institutional Research Committee and Institutional Ethical Committee (REF NO: PRIMS/IEC-NO:58) on 21.02.2018. The required sample size calculated by the power of the study is 80% ($\beta = 0.2$) with 95% of confidence ($\alpha = 0.05$) and the effect size is 0.4 based on the exposure index parameter, it has to be 200 samples (100 in biomass fuel user group and 100 in clean fuel user group).

The participants were selected for the two groups by convenience sampling method. The households were visited to identify the demographic details – age, family history – married or unmarried, number of children, medical history – medication for any diseased condition, known cardiovascular diseases, respiratory illness, cooking profile – type of cooking fuel, house type, location of kitchen and ventilation type.

The included participants of both groups were healthy females in the age of 18 – 50 years using biomass fuel or clean fuel with a minimum of 4 hrs/day and 5 years duration of exposure. Exclusion of study participants from this study which is based on pregnant and lactating women, known cardiovascular diseases, known respiratory illness, smokers, and medication for any diseased conditions.

Participants were provided with detailed information about the study purpose, procedures, risks, benefits, and their rights. The participant can ask questions and make an informed decision about their participation. The

participant's information was reserved confidentially as documents. Signed informed consent was obtained from each participant before performing the test.

The height of the participants was measured by using the stadiometer. The weight of the participants was recorded by the weighing machine. BMI was calculated by weight and height and recorded as data. The test procedures were done between 8 am to 3 pm to avoid the diurnal variation in the hospital.

The pulmonary function test parameters were forced vital capacity (FVC), forced expiratory volume in 1st second (FEV_1), FEV_1/FVC ratio, forced mid-expiratory flow ($FEF_{25-75\%}$), peak expiratory flow rate (PEFR) recorded by computerized Spirometer (RMS – Helios 401). Before performing the pulmonary function test, the procedure was explained along with the purpose and importance of measurements given to the subject. Subjects blow out as hard and fast as possible into the spirometer immediately after the deep inhalation in sitting upright position with feet flat on the floor. Subjects were asked to maintain a good seal around the mouthpiece with their lips. The measurement was repeated a minimum of three times and recorded the highest value for tabulation.

The participants were enrolled in the hospital on the day of the visit, after enrolment 3 ml of venous blood was taken in a syringe and collected in an EDTA (anticoagulated) test tube. The sample was transported to the testing lab (CVR labs (p) limited) in the freezer (-20°C or -80°C) to analyze the metals [Mercury (Hg), Cadmium (Cd), Chromium (Cr), Nickel (Ni), Zinc (Zn)] by the method of Inductively Coupled Plasma Mass Spectrometry (ICP-MS). This instrument is highly sensitive and allows detection of elements at extremely low

concentrations. The liquid sample is converted into aerosol then changed to ionize and focused into mass spectrometer. Separated ions are detected and quantified based on their mass-charge (m/z) ratio.

Serum CC16 protein secretion was measured by quantitative sandwich enzyme immunoassay technique. 3 ml of venous blood was taken and collected in a serum separator tube after enrolment of the subject in the hospital. The sample was transported to the testing lab in a freezer (-20°C or -80°C) to analyze Club cell-16 protein (CC-16) by ELISA method (Cusabio Biotech Co Ltd). The detection range was 6.25 ng/ml – 400 ng/ml and Sensitivity was < 1.56 ng/ml for this instrument.

Data was tabulated in MS Excel & Statistical analysis of the data was done using SPSS software 20 version.

The normality of data was checked by the Kolmogorov-Smirnov test. Age, weight, BMI, FEF_{25-75}%P, Zinc, and CC16 protein secretion were normally distributed. Height, exposure index, FVC, FEV1, FEV1/FVC, FEF_{25-75}, PEFR, Cadmium, Mercury, Chromium, and Nickel parameters were not normally distributed. Normally distributed data are represented as mean and standard deviation (mean±SD) and the data that were not normally distributed are represented as box plots showing medians and inter-quartile ranges (IQR).

A test of significance was performed using Student's t-test for parametric parameters and the Mann-Whitney U test for non-parametric parameters.

Covariate-adjusted test (Univariate analysis) was performed for the comparison of parametric parameters after control of age, height, weight, and

BMI. Quade's test was performed for the non-parametric parameters after control of covariates such as age, height, weight, and BMI.

The correlation analyses were performed by Pearson correlation for parametric parameters and Spearman correlation for non-parametric parameters.

Partial correlations were applied for correlations between parameters, after adjusting the age, height, weight, and BMI.

p values <0.05 was considered statistically significant.

Result

The effect of transition metals from biomass fuel smoke on lung volumes and CC16 protein secretion was assessed in healthy rural females using biomass fuel and the data was compared with healthy females using clean fuel for cooking or other heating purposes in the age of 18 to 50 years.

The samples included 100 in the study group as the biomass fuel group and 100 in the control group as the clean fuel group. Most rural women were living in the pukka house in the same area using the kitchen with proper ventilation. Many of them are moderately educated. Both the group of participants have been exposed to their respective cooking fuels for a minimum of 5 years at an average of 4 hours per day. On history taking, the participants had no complaints of respiratory or cardiovascular disease or any other illness or no medication for other disease conditions, no pregnancy and lactating.

The demographic data such as age, height, weight, BMI show significant differences between the biomass fuel group and the clean fuel group. The exposure index (Hr-yr) was significantly higher in the biomass fuel group than in the clean fuel group ($p<0.001$*).

The comparison of serum concentration of transition metals levels were cadmium (p 0.011*), nickel ($p <0.001$*), and chromium ($p <0.001$*) significantly higher in the biomass fuel group than in the clean fuel group but the serum mercury level was lower in biomass fuel group than clean fuel group. The Serum concentration of Zinc (p 0.533) showed no significant difference between the biomass fuel group and the clean fuel group. In Quade's test, after

controlling the covariates (age, height, weight, and BMI) nickel (p 0.030*) and chromium (0.0001*) show a significant difference between the two groups.

The comparison of observed value of Pulmonary Function between two groups in FVC (p <0.001*), FEV_1 (p <0.001*), FEV_1/FVC (p <0.001*), FEF_{25-75} (p <0.001*), PEFR (p <0.001*) were significantly lesser in the biomass fuel group than the clean fuel group and in percentage predicted value of pulmonary function in FVC (p <0.01*), FEV_1 (p <0.001*), FEV_1/FVC (p <0.001*), FEF_{25-75} (p <0.001*), PEFR (p <0.001*) were significantly lesser in the biomass fuel group than the clean fuel group. In Quade's test, after controlled the covariates (age, height, weight, and BMI) the pulmonary function parameter FEV_1 (p 0.0001*), FEV_1/FVC (p 0.0001*), FEF_{25-75}(p 0.001*), PEFR(p 0.001*) shows the significant difference and the covariate-adjusted test shows a significant difference in $FEF_{25-75\%}$P (p 0.001*) between the biomass fuel group and the clean fuel group after adjusting the covariates – age, height, weight, and BMI.

Correlation between transition metals and observed value of pulmonary function shows a significantly negative correlation of mercury with FVC, and PEFR; nickel with FEV_1/FVC% among biomass fuel group and correlation between transition metals and percentage predicted value of pulmonary function shows a significantly negative correlation of mercury with PEFR; nickel with FEV_1/FVC% among biomass fuel group.

Partial correlation between serum transition metals and the observed value of pulmonary function after controlling age, height, weight, and BMI shows a negative correlation of mercury with PEFR (r = -0.250, p = 0.014); chromium with FEF_{25-75} (r = -0.245, p=0.016) for the biomass fuel group.

Partial correlation between serum transition metals and percentage predicted value of pulmonary function after controlling age, height, weight, and BMI shows a negative correlation of mercury with PEFR %P ($r = -0.249$, $p = 0.014$); and FEF_{25-75}%P ($r = -0.253$, $p=0.013$) for the biomass fuel group.

A comparison of S-CC16 protein secretion (ng/ml) concentration shows no significant difference between the biomass fuel group and the clean fuel group but S-CC16 secretion was higher in both groups (213.4±103.8 and 233.1±112.7) compared with normal serum concentration level.

The comparison of CC-16 protein secretion (ng/ml) between two groups by covariate-adjusted test shows no significant difference between the two groups after adjusting the covariates.

Correlation between the transition metals with CC-16 protein secretion shows no significant relation between the two groups. The partial correlation after controlling age, height, weight, and BMI shows no correlation between transition metals and CC-16 protein secretion among the biomass fuel group.

The observed value and percentage predicted value of pulmonary function correlate with CC-16 protein secretion shows no significance among the biomass fuel group and also no significant correlation by partial correlation among the biomass fuel groups.

Discussion

In the present study, we aimed to analyze the effect of transition metals which are contained in biomass fuel smoke on respiratory parameters. The participants (200) used biomass fuel as wood and clean fuel as LPG for energy purposes for a minimum of 3 years to a maximum of 50 years with the age group - 18 to 50 years of healthy adult. The house type of all participants was a pucca house with good ventilation in the kitchen. A biomass exposure index (BEI) was defined to compare the clinical and functional parameters of the subjects with the exposure time of biomass. It is calculated as the average hours spent during daily cooking multiplied by the number of years and expressed as hour-years (Hr -Yrs).

The biomass exposure index (BEI) for biomass fuel users was found to be 75(46.5,90) which was higher than the clean fuel user whose exposure index was 45(30-60), this is similar to another study[11] showed BEI much higher for biomass fuel users (63.79±36.55) than the clean fuel users due to biomass fuel has less energy content per kg of fuel[12].

The duration of cooking is more in the biomass fuel group which showed significantly lesser in observed and percentage predicted values of pulmonary function test: FVC, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$, PEFR than the clean fuel group which is similar to another study may be due to chronic inhalation of respirable particles (<10µm) that can easily penetrate and deposit in pulmonary airways and lung parenchyma, it may have more potential for damaging lung function among rural women[13].

Chromium concentration in serum level was significantly higher in the (32.03 µg/dl) biomass fuel group than in the clean fuel group (16.60 µg/dl). Partial correlation showed that Chromium had a significant negative correlation with an observed value of FEF_{25-75} (r =-0.245, p=0.016) and FEF_{25-75}%P (r =-0.253, p=0.013) after controlling the confounders such as age, height, weight, BMI among biomass fuel group. Similarly, another study found that lesser pulmonary function parameters [FVC 77.2±12.0, FEV_1 65.8±10.1, FEV_1/FVC 63.9±12.3, $FEF_{25-75\%}$ 73.6±9.3], the mean chromium levels were higher in both urine (31.1±7.9µg/g creatinine) and breathing zone air (63.0±11.6 µg/m^3) among the production section of tannery workers than the control group due to the formation of free radicals during the intracellular reduction of chromium may affect pulmonary function[14].

Mercury concentration in serum level was lower in the biomass fuel group (1.38µg/dl) than in the clean fuel group (2.01µg/dl). Partial correlation showed that Mercury had a significantly negative correlation with observed value of PEFR (r = -0.250, p = 0.014) and in PEFR %P (r = -0.249, p = 0.014) among biomass fuel group after controlling the confounders such as age, height, weight, BMI. Similarly, another study found that mercury concentration was significantly higher in pulmonary ventilation dysfunction (PVD) (314.21±196.03 µg/dl) than in non-PVD (0.13±0.11 µg/dl) and mercury was negatively correlated with FEV1% and FVC% after adjusted covariates among solid fuel users. Mercury can evaporate even at ordinary temperatures and can easily absorbed through mucous membranes and oxidized which can affect pulmonary function[15].

Cadmium concentration in serum level was significantly higher in the (0.28µg/dl) biomass fuel group than the clean fuel group (0.10µg/dl). In partial correlation between Cadmium and pulmonary function showed no significant correlation among the biomass fuel group after controlling the confounders such as age, height, weight, and BMI but contrary to another study due to the protective role of zinc against cadmium toxicity because of both metal ion has similar properties[16].

Zinc concentration in serum level was no significant difference between the biomass fuel group (784.38 ± 252.8 µg/dl) and clean fuel group (757.08 ± 306.8 µg/dl). In partial correlation between zinc and pulmonary function showed no significant correlation among the biomass fuel group after controlling the confounders such as age, height, weight, and BMI contrary to another study that found that increased urinary zinc (312 µg/L) is associated with restrictive ventilatory impairment due to a decline in FVC and FEV_1 rather than obstructive ventilatory impairment but the association between zinc exposure and lung function is complex because zinc acts as both nutritious and toxic[17].

The median nickel concentration in serum level was significantly higher in the biomass fuel group (41.86 µg/dl) than in the clean fuel group (29.63 µg/dl). Nickel had no association with pulmonary function in partial correlation after control confounders such as age, height, weight, and BMI in the age group of 39.91±8.45 yrs among women, which is contrary to another study Jun-Pyo Myong et al found that the increased serum nickel concentration (0.310 µg/L) was associated with reduced FEV_1 and $FEF_{25-75\%}$ among Korean men aged 40 or older (57.3±10.9 yrs) but no association with females aged 40 or older (55.8±10.0 yrs) due to females are protected from nickel toxicity through a

decrease in the female hormone (progesterone and 17 beta-estradiol), which is involved in the inhibition of the expression of metallothionein (MT) mRNA[18].

The serum CC16 protein was not significantly different between the biomass fuel group (213.4±103.9 ng/ml) and the clean fuel group (233.1±114.2 ng/ml) and no significant partial correlation with pulmonary function and transition metals in the age of 18 – 50 yrs. Contrary to another study by Rong et al (2020) found that S-CC16 protein concentration was lesser in stable COPD (stage of GOLD-3 to 4) than the controls (94.2±20.9 Vs 111.3±17.9 ng/ml) in the age of 46 – 77yrs with the decline in FEV_1 /FVC and FEV_1%[19] and Lin et al (2020) found that S-CC16 protein was higher in ARDS than in the control group (47.78±19.92 Vs 22.23±13.28 ng/ml) with decreased albumin and increased creatinine concentration and NT- proBNP levels in critical care unit patients[20].

In our study, both obstructive and restrictive disease patterns are seen. Obstructive diseases lead to club cell cytotoxicity decreasing the concentration of S-CC16 protein secretion. Epithelial permeability increases in restrictive diseases increasing the concentration of S-CC16 levels.

Summary and conclusion

In developing countries, women have used wood stoves for cooking and exposed to smoke for years. Biomass fuel can cause a decline in pulmonary functions due to suspended particles in smoke. The biomass smoke has various particles as particulate matter. Our study findings tell that higher concentrations of transition metals released from biomass fuel combustion as a suspended particle which predominantly affect the pulmonary function among rural women and also interfere with the protective effect of CC-16.

Further research is recommended to analyse the toxicity of transition metals on the concentration of serum CC16 protein and CC16 protein in BALF to clarify pulmonary function. The expanded research will provide a better quality of individual life who are exposed to biomass smoke pollutants.

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PAPER PUBLICATION – 1

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Research Article

A comparative analysis of biomass and clean fuel exposure on pulmonary function during cooking among rural women in Tamilnadu, India

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Declaration on official E-mail:
The corresponding author declares that an official e-mail from the institution is not available for all authors.

Abstract:
It is of interest to document data on the comparative analysis of biomass and clean fuel exposure on pulmonary function during cooking among rural women. The study consisted of 100 biomass and 100 LPG fuel using women with no smoking habits and other related illness Parameters such as FVC, FEV_1, FEV_1/FVC, PEFR, $FEF_{25-75\%}$were obtained using the computerized spirometry to assess the pulmonary function in these subjects. The collected data were analyzed using the Student t-test method and Pearson correlation. The exposure index for biomass fuel users is 69.78±27.25 showing high exposure duration during cooking. The parameters for pulmonary functions significantly declined in FVC (42.34±13.6), FEV_1 (45.55±15.98), PEFR (34.11±14.78) and $FEF_{25-75\%}$ (45.56±23.00) for biomass fuel user. However, this is not true for FEV_1/FVC ratio (107.56±16.9). The increase in PFT suggests the restrictive and obstructive patterns of pulmonary diseases. There was a negative correlation between increased duration of cooking and the value of FEV_1/FVC (r = -0.2961), $FEF_{25-75\%}$ (r = -0.3519) and PEFR (r = -0.2868). Thus, the deformation of pulmonary function due to extended exposure of biomass fuel for

PAPER PUBLICATION – 2

Original Article

Effect Of Biomass Exposure Index On Club Cell Protein In A Pulmonary Epithelial Cell Among Rural Cooking Women

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Abstract

Background: The club cell protein is secreted in terminal bronchioles, which have a protective role in the lungs. This study explains the potential influence of persistent exposure to wood smoke on club cells in the lungs among rural women in Tamil Nādu, India. **Methodology:** A comparative study between wood fuel users and LPG fuel users among 200 healthy rural women was conducted in Kancheepuram district, Tamil Nādu, India.Based on age (18-55 yrs) and the women had undergone clinical evaluation before the test. Detailed information about anthropometry data, the ventilation profile, the duration of cooking, and the history of any diseased condition or smoking were collected for both groups. The exposure index is calculated for both groups. Under aseptic precautions, the pulmonary inflammatory marker: club cell – 16 proteins in serum were estimated by ELISA for both groups. **Results:** The Mann-Whitney U test was used to analyze the data.The two groups exhibited significant differences in age (**p 0.003**), height (**p 0.000**), weight (**p 0.000**), and BMI (**p 0.000**). The exposure index was significantly higher among wood fuel users (**p <0.000**). The median value of the exposure index in the box plot diagram shows higher value for the wood fuel user than the clean fuel user. The club cell protein/CC-16 protein (ng/ml) secretion shows no significant difference (**p 0.122**) between the two groups but the median value of the box plot was lower for wood fuel users than LPG fuel users. Negative correlation between exposure index and CC-16 protein secretion for wood fuel user. **Conclusion:** Prolonged use of wood as a fuel for cooking affects the club cell protein secretion in the lungs among rural women which causes various pulmonary diseasescompare to those using LPG.

Keywords: wood fuel, biomass exposure index, club cell protein, lung epithelial barrier.

INTRODUCTION

A club cell is a non-ciliated, non-mucous secreting club-shaped cell and it has a dome-shaped luminal surface and electron-dense cytoplasmic granules.[1] Protein has a molecular mass of 16,000 daltons [2] and belongs to the secretoglobin subfamily. The club cell protein is homodimeric with 70 amino acids lined in an antiparallel manner by two disulfide bonds.[3] Club cell protein (CC16) is distributed throughout the tracheobronchial tree, particularly in the terminal bronchioles where club cells are found, and is also found in other organs such as the prostate, ovaries, pancreas, mammary gland, and the uterine endometrium.[4]

PAPER PUBLICATION – 3

Variability of Pulmonary Function Associated with Serum Nickel in Women Exposed to Clean and Biomass Fuel in a Rural Tamil Nadu

Section A-Research paper

Variability of Pulmonary Function Associated with Serum Nickel in Women Exposed to Clean and Biomass Fuel in a Rural Tamil Nadu

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Abstract

Background: Indoor air pollutants are constituted by organic compounds, polyaromatic hydrocarbons, transition metals like nickel, chromium etc from biomass smoke, which alter the pulmonary ventilation. Explaining the effect of metal function on pulmonary among cooking women is very minimal. We evaluated the effect of nickel on pulmonary functions among biomass fuel users in rural areas. **Methodology**: 200 healthy subjects selected biomass fuel use and LPG fuel use from the rural area of Kancheepuram District in India. Written consent and demographic data were collected from every participant before the performance of the test. Pulmonary function tests were done by a computerised Spirometer to assess the FEF_{25-75}% and PEFR% parameters. Serum Nickel was estimated in blood by ICP-MS technology. We used multivariate statistical analysis to find the variation on pulmonary function due to the effect of nickel among biomass fuel users. **Results and findings**: PEFR% (34.63±14.90; 41.92± 15.70, p **0.025**) shows significant difference between biomass fuel user and LPG fuel user for the subgroup of <35(µg/dl) nickel concentration. $FEF_{25-75\%}$ (43.87±23.61; 55.28±17.32, p **0.014**) and PEFR% (33.81±14.82; 40.08±12.68, p **0.037**) shows significance difference between biomass and clean fuel users for the subgroup of >35(µg/dl) nickel concentration. After adjustment of BMI, $FEF_{25-75\%}$ and PEFR (p **0.012**; p **0.026**) were showed the significant difference between biomass and clean fuel users for the subgroup of >35(µg/dl) nickel concentration and the variability for $FEF_{25-75\%}$ and PEFR was 6.3% and 5.1%. **Conclusion**: Our study concludes that